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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/654,763	09/03/2003	Nicholas P. Barker	50206/014002	6915

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/654,763	BARKER ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/29/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

During a telephone conversation with Paul Clark on 2/21/2006, a provisional election was made, without traverse, to prosecute claims 11-20. However, upon further consideration, the Examiner has determined that the subject matter of claims 1-10 and 21-23 is not distinct from that of claims 11-20, and any search for the subject matter of claims 11-20 would overlap with the search required for claims 1-10 and 21-23. Therefore, claims 1-23 will be examined together and are the subject of this Office Action.

Information Disclosure Statement

The information disclosure statement received on 6/29/2004 has been fully considered by the Examiner.

Specification

The use of the trademarks Wellferon, Alferon, Multiferon, and Infergen (p. 4, lines 2-8) has been noted in this application. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The metes and bounds of the term "asialo-interferon" are not clear. The

specification, on page 5, lines 5-6, defines an asialo-interferon as "a glycosylated interferon lacking a terminal sialic group that is present in the native glycoslylated interferon." Pages 12-15 of the specification describe methods of producing asialo-interferons, including recombinant methods, and on page 13, line 26 – page 14, line 1, states that the precise host cell used to produce interferons is not critical to the invention. It is known in the art, however, that not all host cells sialylate recombinant proteins. For example, some insect and plant cells are known to produce non-sialylated recombinant proteins (Marchal *et al*, 2001, Biol. Chem., Vol. 382, pages 151-159; Altmann *et al*, 1999, Glycoconjugate J., Vol 16, pages 109-123; Sugyiami *et al*, 1993, Eur. J. Biochem., Vol 217, pages 921-927; Goochee *et al*, 1991, Bio/Technology, Vol. 9, pages 1347-1355). Additionally, the yeast *Saccharomyces cerevisiae* lacks the enzymes β1,4 galactosyltransferase and α2,6 sialyltransferase, and glycans from *S. cerevisiae* lack galactose and sialic acid residues (Krezdorn *et al*, 1994, Eur. J. Biochem., Vol. 220, p. 809-817). Thus, asialo-interferons can be produced by methods disclosed in the specification, or via recombinant methods in a host cell incapable of sialylation. Furthermore, given the broadest reasonable interpretation, the claims, which do not define or limit the type or source of the claimed asialo-interferon(s), read on any interferon lacking a terminal sialic acid residue. For the purposes of examination, the examiner has interpreted "asialo-interferon" as any interferon, from any source, that lacks a terminal sialic acid residue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-13 and 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi (US 6,296,844 – cited in Applicants information disclosure statement) in view of Trere *et al* (Br. J. Cancer, 1999, Vol. 81, pages 404-408 – cited in Applicants information disclosure statement), and further in view of Treiber (Digestive Diseases, 2001, Vol. 19, pages 311-323 – cited in Applicants information disclosure statement). The claims of the instant invention are drawn to a method for treating a patient having liver cancer, said method

comprising testing said liver for expression of an asialo-glycoprotein receptor, and if the testing step indicates presence of the receptor, administering an effective amount of an asialo-interferon. Takahashi discloses administration of human asialo-IFN, including IFN-α, IFN-β, and IFN-γ, as a treatment for liver disease (column 1, lines 63-67, and claims 1, 10-18, 23). Takahashi also teaches that asialo-IFN is more effective than native IFN in treating disease because of the prevalence of asialoglycoprotein receptors on hepatocytes (column 4, lines 57-61), and because of this higher specificity, higher doses of asialo-IFN are possible with lower toxicity (column 16, lines 49-50). Furthermore, Takahashi teaches that other diseases, notably hepatocellular carcinoma, can be treated by administration of other asialo-cytokines (column 3, lines 5-16). Takahashi does not teach methods of testing liver tissue for presence of asialo-glycoprotein receptors, or co-administration of asialo-IFN with additional anti-neoplastic therapy.

Trere *et al* teaches a method for determining the presence of asialo-glycoprotein receptors on hepatocytes, with said method comprised of performing a liver biopsy (p. 405 – Materials and Methods). Trere *et al* also teaches that asialo-glycoprotein receptors are overexpressed on human hepatocellular carcinoma cells compared to healthy liver tissue (p. 405, last paragraph – p. 406, 1st column, and Figures 1-2).

Treiber discloses numerous types of therapy for treatment of hepatocellular carcinoma, including surgical procedures, chemotherapy, and radionuclide therapy (Table 1). Treiber also teaches interferon therapy as a treatment for hepatocellular carcinoma (p 312, 1st column), and also discloses interferon therapy combined with various chemotherapeutic agents (p. 313-314).

It would have been obvious to a person of ordinary skill in the art, at the time the invention was made, to treat liver cancer by a method comprised of testing liver cancer for the presence of asialoglycoprotein receptors, and if said receptors are present, administering an asialo-interferon. The motivation to do so is given by Takahashi, which teaches administration of asialo-interferons for treatment of liver disease, and Treiber, which teaches treatment of hepatocellular carcinoma with interferons, and also teaches administration of interferons with additional anti-neoplastic therapy. The motivation to determine asialoglycoprotein receptors is provided by Trere *et al*, which teach that the receptors are overexpressed in liver cancer, and also teach a biopsy-based method for determining receptor levels. One of ordinary skill in the art, therefore, would have both the motivation to follow the teachings of Takahashi, Treiber, and Trere *et al*, but also a reasonable expectation of success in practicing the methods of the instant invention.

2. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi, in view of Kudo et al (J. Nuc, Med., 1991, Vol. 32, No. 6, p. 1177-1182), and further in view of Treiber. The subject matter of the instant application, and the teachings of Takahashi and Treiber are discussed above. Kudo *et al* teaches a method of *in vivo*, non-invasive determination of asialoglycoprotein receptor levels (see p. 1178, 1st column).

It would have been obvious to a person of ordinary skill in the art, at the time the invention was made, to treat liver cancer by a method comprised of testing liver cancer for the presence of asialoglycoprotein receptors, and if said receptors are present, administering an asialo-interferon. The motivation to do so is given by Takahashi, which teaches administration of asialo-interferons for treatment of liver disease, and Treiber, which teaches treatment of hepatocellular carcinoma with interferons. The motivation to determine asialoglycoprotein receptors is provided by Kudo *et al*, which teach an *in vivo*, non-invasive method for determining receptor levels. One of ordinary skill in the art, therefore, would have both the motivation to follow the teachings of Takahashi, Treiber, and Kudo *et al*, but also a reasonable expectation of success in practicing the methods of the instant invention.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BDH
Art Unit 1646

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER